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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/417,478	10/13/1999	JOHN MCCAFFERTY	05569.0004.DVUS07	8812

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EXAMINER

LIU, SUE XU

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/417,478	MCCAFFERTY ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/31/03;11/25/02</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Please note the change of examiner for this application. (Please see the Conclusion paragraph for information on any future correspondence.)

Claim Status

Claims 44-53 are currently pending;

Claims 44 and 45 have been amended as filed on 5/21/2001 and 9/7/2000 respectively;

Claims 44-53 are being examined in this application.

Information Disclosure Statement

1. The documents listed in the information disclosure statements filed on 7/31/2003 and 11/25/2002 are considered. However, the documents that are not patent and/or literature publications (such as Court Documents, Research Agreements, Research Grant, etc.) are crossed out from the IDS (See the attached PTO 1449), and will not be published if the instant application is found to be allowable.

Drawings

2. The following regarding informal drawings are noted in the previous office action (11/20/2000; pg 2):

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Art Unit: 1639

Applicant is invited to notice that boxes 2, 6 and 12 were checked by the draftsman in PTO 948. Applicant is encouraged to amend the specification so that the description of renumbered figure corresponds to the renumbered figures.

Applicant's request of holding the formal drawing requirements in abeyance until allowance is acknowledged.

Specification

3. In the previous office action (11/20/2000), it is noted that the trademarks used in the instant specification have not been capitalized.

Applicants state in the reply (filed on 5/21/2001) that a supplemental amendment will be filed to amend the instant specification regarding the usage of trademarks. However, it is noted that a supplemental amendment has not been filed.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

5. Claims 44 and 46, as amended or originally filed, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

Art Unit: 1639

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record advanced on pages 3-6 of the office action mailed on 11/20/2000.

Discussion and Answer to Argument

6. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record):

Distinction between "written description rejection" and "scope of enablement rejection"

In the reply filed on 5/21/2001, applicants have addressed both the "written description" and "scope of enablement" rejections together and have formulated the traversal argument as such. However, the court has affirmed that written description requirement is separate and distinct from the enablement requirement under 35 U.S.C. 112, first paragraph. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19; USPQ2d 1111, 1115 (Fed. Cir. 1991) and MPEP 2161.

For the sake of clarity, applicant's arguments are addressed separately in terms of "written description" and "scope of enablement". Only the relevant arguments (as best understood by the examiner) to written description are discussed in this section, and applicant's arguments pertaining to "scope of enablement" are addressed later in this office action.

Applicant's arguments over the written description rejection

I. Applicants argue that “any person of ordinary skill in the art reading the specification will note that various techniques for generation of genetically diverse populations have been described” (pg 5, 2nd para. of applicant’s reply).

II. Applicants also argue that it is fundamentally wrong that the skilled artisan cannot envision the method of making the libraries of other specific binding pairs which would be displayed on the surface of a filamentous phage (pg 5, 3rd para. of applicant’s reply).

III. Applicants also argue that a claimed invention need not be described *ipsis verbis* in order to satisfy the requirements of 35 U.S.C. §112 (pg 5, 4th para. of applicant’s reply). Applicants have pointed to several examples in the instant specification to indicate support for the claimed invention (bottom of pg 5 and pg 6 of applicant’s reply).

IV. Applicants conclude that “irrespective of the nature of the polypeptide, the essentially the same methods can be used to mutate non-antibody polypeptides, and these methods are fully disclosed in the specification as filed” (see pg 7 of applicant’s reply).

Answer to applicant's arguments

Overall, applicants traverse the written description rejection by demonstrating that the instant specification does provide adequate written description to generate a genetically diverse population.

First, these arguments are irrelevant to the written description rejection over the claimed genus of “binding pairs”. The written description rejection set forth in the previous office action is directed to the genus of “binding pairs” as encompassed by the instant claim. That is the instant specification does not provide sufficient written description to show possession of the entire genus of binding pairs as discussed in the previous office action. The instant specification on page 27 defines that a specific binding pair is “a pair of molecules which are naturally derived

Art Unit: 1639

or synthetically produced”. Thus, any two molecules (including diverse molecules that are not antibodies such as hormone-receptor, enzyme-substrate, biotin-avidin, etc.) that can bind to each other would read on the specific binding pair. However, the instant specification only discloses examples of one type of specific binding pair, antibodies. Antibody binding pairs do not constitute representative number of species for the entire genus of “binding pair” and/or provide common structural limitation for the entire claimed genus.

Second, the examples from the instant specification pointed out by the applicants only demonstrate one single species of “binding pair” (i.e. antibody binding pair) and are not representative of the entire genus of any binding pair. Specifically, Examples 17-19, 24-27, 33, 38, 44, and 45 listed by the applicants on pgs 5-6 of the reply are all examples of single chain antibodies or antibodies expressed on the surface of phage particles. These Examples disclosed in the instant specification do not describe other binding pairs (that are not antibodies) expressed on the surface of phage particles.

Applicants also cited Example 32 as an example to show that the specification does disclose other proteins or molecules that are expressed on the surface of phage. However, Example 32 does not show the expression of a “binding pair” on the surface of phage. Example 32 only discloses the expression of one single enzyme (alkaline phosphate) that does not comprise a “binding pair”.

Applicants also pointed out pgs 13, 14 and 22 of the specification disclose phage displaying both antibody and other polypeptides (such as enzymes). These disclosures do not provide description of other species of “binding pair”. Examples of displaying other enzymes that are not “binding pair” do not provide support for the claimed genus of “binding pair”.

Third, applicant's argument regarding the demonstration of techniques to mutate proteins to create genetically diverse populations is irrelevant to the written description rejection. Mutations of antibodies would not produce "binding pairs" that are not antibody binding pairs. Phage displaying mutated antibodies (binding pairs) are still antibodies, but not other proteins or molecules that can be construed as binding pairs. The mutation methods described in the specification would also not lead to other "binding pairs" that can be displayed on the surface of phage.

Therefore, applicant's traversal over the written description rejection is found not persuasive, and the rejection is still maintained.

Scope of Enablement Rejection

7. Claims 44 and 45, as amended or originally filed, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recombinant cells harboring library of specific binding pair member comprising single chain antibody, does not reasonably provide enablement for recombinant cells harboring any other specific binding pair members. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record advanced on pages 6-7 of the office action mailed on 11/20/2000.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record):

Applicant's arguments over the written description rejection

I. Applicants argue that the examiner's contention of the skilled artisan cannot envision the method of making libraries of other specific binding pairs which would be displayed on the surface of a filamentous phage is "a completely unsubstantiated assertion, without reliance on any technical facts or evidence" (pg 4, 2nd para. of applicant's reply).

II. Applicant also argues "a disclosure need not teach, and preferably should omit, what is well known to those of skill in the art." (pg 4, 3rd para. of applicant's reply).

III. Applicants also argue "as long as the specification contains at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claimed invention, then the enablement requirement under 35 U.S.C. §112 is satisfied." (pg 4, 3rd para. of applicant's reply).

IV. Applicants also argue that the specification provides methods for in vitro and in vivo mutagenesis, and for generation of genetically diverse populations (pg 4, last para. and pg5, 1st para. of applicant's reply).

Answer to applicant's arguments

Similar to applicant's argument over the written description requirement, applicants have misinterpreted the enablement rejection as directing to the scope of generation of a genetically diverse population, but not the scope of the claimed "binding pair".

First, applicant's argument (IV from above) that the specification provides methods for generation of genetically diverse populations is irrelevant to the scope of enablement rejection. There is no dispute that the various methods and techniques for generating genetic diverse

Art Unit: 1639

populations of proteins (such as antibodies or other polypeptides) are either demonstrated by the instant specification or are known in the art. However, the question is whether the specification enables one skilled in the art to generate any binding pair that is expressed on the surface of phage particles. The only examples provided in the specification are phage displaying antibodies (one single species of a binding pair that is displayed by phage). Although the specification provides examples of phage displaying other molecules (enzymes), no other examples of “binding pairs” are provided. The examples of enzymes recited in the instant specification do not constitute “binding pairs” as defined by the instant specification.

Second, Applicant’s second (II) and third arguments (III) are also not persuasive because methods of displaying “binding pairs” on phage surface were not well known in the art at the time the invention was made, and the method of making single species of a “binding pair” phage display library cannot be reasonably correlated to the entire scope of the claimed invention of any binding pair. As stated in the previous office action (bottom of pg 7), “at the time the invention was made it was not known to make library of compounds other than the polypeptides such as antibodies to display on the surface of the filamentous phage.” Other examples of phage display library known in the art at the time the invention was made are peptide phage display libraries. These peptide display libraries do not constitute “binding pairs”, because only individual peptides are displayed. The methods of making different phage display libraries are not trivial. Considerations such as size of the inserts into the phagemid, and solubility of the inserted polypeptide are all factors that can influence the success of the methods. The success of displaying single chain antibodies (comprising binding pairs) does not automatically translate into successful displaying other binding pairs such as receptor-hormone pairs.

Therefore, the statement of “the skilled artisan cannot envision the method of making libraries of other specific binding pairs which would be displayed on the surface of a filamentous phage”, as recited in the previous office action, is not “a completely unsubstantiated assertion, without reliance on any technical facts or evidence” as argued by the applicant (argument I above). Besides the technical facts and evidences discussed above, the instant specification also provides evidence that phage display cannot be easily generalized to any other proteins. For example, the specification recites an example of an unsuccessful attempt to display a bovine pancreatic trypsin inhibitor using phage (pg 10, line 9+ of the instant specification).

In conclusion, the instant specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make recombinant cells harboring any specific binding pair members beside antibodies.

New Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 44-53 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This new rejection is necessitated by applicant's amendment to the claims as filed on 5/21/2001.

Art Unit: 1639

Claim 44 is amended to recite “recombinant host cells which each harbor a nucleic acid fragment encoding a specific binding pair member”. It is not clear if each of the recombinant cell comprises one member of the binding pair or if it comprises both members of the binding pair.

Claim 44 is also amended to recite “...bacteriophage particles and comprise a binding domain...” on line 7 of the claim. It is not clear of what entity the said “a binding domain” is comprised. The claim language can be interpreted to mean the “specific binding pair members” comprise a binding domain, or the “bacteriophage particles” comprise the binding domain.

Claim 44 is also amended to add a comma between the phrase “...binding pair member” and “and genetic material” on line 8 of the claim. It is not clear of what entity the “genetic material” is comprised.

Claim 44, in general, is so unclear, convoluted and confusing, that one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

Art Unit: 1639

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PETER PARAS, JR.
PRIMARY EXAMINER

Pete Paras
SPE 1639

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Art Unit 1639
6/22/2006